

# Regulatory Education for Industry (REdI): PRESCRIPTION DRUG LABELING CHALLENGES AND ISSUES

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# Distributing Specific Population Information in Labeling

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- ➤ The views and opinions expressed in this presentation represent those of the presenter, and do not necessarily represent an official FDA position.
- ➤ The labeling examples in this presentation are fictitious and are provided only to demonstrate current labeling development challenges.

# Distribution of Renal Impairment Information: Example <u>Overview</u>

#### 2 DOSAGE AND ADMINISTRATION

The recommended once daily oral dosage of DRUG-X is:

- 25 mg in patients with normal renal function or mild renal impairment (i.e., creatinine clearance between 60 to 90 mL/minute as estimated by Cockcroft-Gault).
- 12.5 mg in patients with moderate or severe renal impairment (i.e., creatinine clearance less than 60 mL/minute as estimated by Cockcroft-Gault) [see Use in Specific Populations (8.6)].

#### 8 USE IN SPECIFIC POPULATIONS

### 8.6 Renal Impairment

The use of DRUG-X in patients with moderate or severe renal impairment was associated greater blood levels of drugoxide compared to patients with normal renal function [see Clinical Pharmacology (12.3)]. Given that increased drugoxide blood levels increases the risk of Adverse Reaction-Y, a dosage reduction in patients with moderate or severe renal impairment (i.e., creatinine clearance less than 60 mL/minute) is recommended [see Dosage and Administration (2)]. A dosage reduction in patients with mild renal impairment is not needed.

#### 12 CLINICAL PHARMACOLOGY

#### 12.3 Pharmacokinetics

### Specific Populations

Patients with Renal Impairment: Compared to patients with normal renal function, the AUC of drugoxide was increased X%, Y%, Z% in patients with mild renal impairment [creatinine clearance (Clcr) 60 to 90 mL/minute], moderate renal impairment (Clcr 30 to 60 mL/minute), and severe renal impairment (Clcr less than 30 mL/minute), respectively, following a single 25 mg dose of drugoxide In addition, the Cmax of drugoxide was increased A%, B%, C% in patients with mild, moderate, and severe renal impairment, respectively [see Dosage and Administration (2) and Use in Specific Populations (8.6)].



## Distribution of Renal Impairment Information Example: Subsection 12.3

### 12 CLINICAL PHARMACOLOGY 12.3 Pharmacokinetics

### Specific Populations

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- Develop data subsections before clinical subsections
- ➤ Describe PK studies and results conducted to identify PK differences in patients with varying degrees of renal impairment relative to PK of drug in patients with normal renal function\*

PK = pharmacokinetics

<sup>\*</sup> Section IV(C)(4) - Clinical Pharmacology Section of Labeling Guidance; Section VI(F) - PK in Patients with Impaired Renal Function - Study Design, Data Analysis, and Impact on Dosing and Labeling Guidance



# Distribution of Renal Impairment Information Example: Subsection 8.6

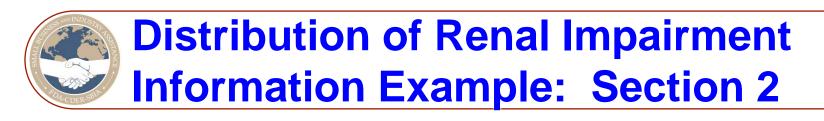
### 8 USE IN SPECIFIC POPULATIONS

### 8.6 Renal Impairment

The use of DRUG-X in patients with moderate or severe renal impairment was associated greater blood levels of drugoxide compared to patients with normal renal function [see Clinical Pharmacology (12.3)]. Given that increased drugoxide blood levels increases the risk of Adverse Reaction-Y, a dosage reduction in patients with moderate or severe renal impairment (i.e., creatinine clearance less than 60 mL/minute) is recommended [see Dosage and Administration (2)]. A dosage reduction in patients with mild renal impairment is not needed.

➤ Describe clinical implications of differences in response, safety, or recommendations for use of drug in patients with renal impairment compared to patients with normal renal function\*

<sup>\*</sup> Section VI(D) - PK in Patients with Impaired Renal Function - Study Design, Data Analysis, and Impact on Dosing and Labeling Guidance



### 2 DOSAGE AND ADMINISTRATION

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- 12.5 mg in patients with moderate or severe renal impairment (i.e., creatinine clearance less than 60 mL/minute as estimated by Cockcroft-Gault) [see Use in Specific Populations (8.6)].
- Must include dosage modifications in D&A section for specific populations\*
- Should include method for calculating creatinine clearance\*\*

<sup>\* 21</sup> CFR 201.57(c)(3)(H); Section II(F) – D&A Section of Labeling Guidance

<sup>\*\*</sup> Section VI(B) - PK in Patients with Impaired Renal Function - Study Design, Data Analysis, and Impact on Dosing and Labeling Guidance



### References

PLR Requirements for Prescribing Information website:

http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm

PK in Patients with Impaired Renal Function - Study Design, Data Analysis, and Impact on Dosing and Labeling Guidance:

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatorylnformation/Guidances/UCM204959.pdf

### Thank you!